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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/668,749	09/23/2003	Hui Wang	10030304-1	2131

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EXAMINER
CLOW, LORI A

ART UNIT	PAPER NUMBER
1631	

MAIL DATE	DELIVERY MODE
05/02/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/668,749	WANG, HUI	
	Examiner	Art Unit	
	Lori A. Clow, Ph.D.	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 April 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,4-15 and 18-35* is/are pending in the application:

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 4-15, and 18-35* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114.

Applicants' response, filed 6 April 2007, has been fully considered. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

Claims 1, 4-15, and 18-35 are currently pending. Claims 2, 3, 16, and 17 have been cancelled.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 4-14, 18, 23-33, and 35 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

In *In re Wands* (8 USPQ2d 1400 (CAFC 1988)) the CAFC considered the issue of enablement in molecular biology. The CAFC summarized eight factors to be considered in a determination of "undue experimentation". These factors include: (a) the quantity of experimentation necessary; (b) the amount of direction or guidance presented; (c) the presence or absence of working examples; (d) the nature of the invention; (e) the state of the prior art; (f) the relative skill of those in the art; (g) the predictability of the art; and (h) the breadth of the claims.

In considering the factors for the instant claims:

a) In order to practice the claimed invention one of skill in the art must be able to perform nanopore data analysis with a nanopore device by providing a sample, generating nanopore data, forming a distribution pattern, analyzing a distribution of the data points and determining at least one of a phosphorylation state, chemical integrity, and ratio of target polynucleotides to non-target polynucleotides, wherein analyzing includes comparing the distribution of target data points between two data clusters to a phosphorylation state standard distribution. For the reasons set forth below, this represents undue experimentation.

b) and c) The specification provides the following with regard to determination of phosphorylation:

In block 38, the relative amount of target polynucleotides to phosphorylated target polynucleotides can be determined. By comparing the scatter plot of the sample of interest to the phosphorylation state distribution standard, the relative amount of target non-phosphorylated polynucleotides to phosphorylated target polynucleotides can be determined. The precision of the relative amounts depends, in part, upon the phosphorylation state distribution standard. For example, if the phosphorylation state distribution standard only includes one scatter plot of the

distribution between the two clusters, then relative ratio of the target polynucleotides to phosphorylated target polynucleotides is less precise than if a plurality of scatter plots of multiple phosphorylation distributions between the two clusters is included in the phosphorylation state distribution standard. As mentioned above, the precision required for a particular analysis can be determined for each analysis. (page 14).

The specification, however, does not provide for comparing the distribution of the target polynucleotide data points between two data clusters to a phosphorylation state standard distribution when the length diversity among polynucleotides or the chemical integrity or ratio of polynucleotides is determined. How is the phosphorylation state standard related to these parameters, if they are the "one" that is determined? For example, if only length diversity is determined, then how are phosphorylation state standards relevant to the claimed method? The specification fails to teach and it is not apparent to one of skill in the art of how to perform such analysis. In claim 26, for example, if only phosphorylation state of the target is determined, then how is the comparison of density distribution and chemical integrity relevant to the claimed method?

d) The invention is drawn to methods of comparing distribution between data clusters to phosphorylation state standard distributions. However, this is not enabled if parameters other than phosphorylation are determined.

e) The art is silent with respect to nanopore analysis and determination of phosphorylation.

f) The skill of those in the art of molecular biology is high.

h) The claims are broad because they are drawn to methods of comparing distribution between data clusters to phosphorylation state standard distributions using other parameters than phosphorylation. The skilled practitioner would first turn to the instant specification for guidance to practice such methods. However, the instant specification does not provide specific guidance to practice these embodiments. As such, the skilled practitioner would turn to the prior art for such guidance, however, the prior art is silent. Finally, said practitioner would turn to trial and error experimentation. Such represents undue experimentation.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 15, 22, 34, and 35 (and claims dependent therefrom) are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 recites, "comparing the distribution of the target polynucleotide data points between tow data clusters to a phosphorylation state standard distribution". It is unclear what the relevance of this step is to the rest of the claim if only a length diversity is determined, for example. What is the relationship of this step with the rest of the claim? Clarification is requested.

Claim 15 recites, "wherein the nanopore data analysis system is further operative to analyze the distribution of the non-target polynucleotide data points, wherein the nanopore data analysis system is further operative to determine a ratio between the target and non-target data

points". It is unclear what the ratio determination has to do with the rest of the claim? What relevance does ratio have to performing a nanopore analysis? Clarification is requested.

Claim 22 recites, "wherein the failure of polynucleotide data points to form at least one cluster indicates that the target polynucleotides in the sample represent less that a calibration specified fraction of the total polynucleotides in the sample. It is unclear what the relationship of the "less than a calibrated specified fraction" is with the nanopore data analysis. What does this represent as a result of the method? Clarification is requested.

Claim 34 recites, "analyze a distribution of target polynucleotide data points between the two data clusters". There is insufficient antecedent basis in the claim for "the two data clusters". Clarification is requested.

Claim 34 recites, "determine the ratio of phosphorylated target polynucleotides to non-target polynucleotides". It is unclear what process is performed to determine the ratio. Is it the determination by comparing the distribution of the standard to both target and non-target? Clarification is requested.

Claim 35 recites, "compare cluster score for the target polynucleotide data points to a cluster score for chemical integrity standard density distribution for the defined area in a distribution of a target polynucleotide standard". It is unclear for what purpose this step is performed. Is it performed to determine chemical integrity? It is unclear what the relevance is of this step to the rest of the claim if in the "determining the at least one of" step only includes determining a ratio, for example. Clarification is requested.

Conclusion

No claims are allowed.

The outstanding rejections under 35 USC 101, non-statutory subject matter, have been withdrawn in view of the claim amendments.

The outstanding rejections under 35 USC 102 have been withdrawn in view of the claim amendments.

Inquiries

Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the PTO Fax Center. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993) (See 37 CFR § 1.6(d)). The Central Fax Center Number is (571) 273-8300.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lori A. Clow, Ph.D., whose telephone number is (571) 272-0715. The examiner can normally be reached on Monday-Friday from 10 am to 6:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on (571) 272-0735.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

April 29, 2007
Lori A. Clow, Ph.D.
Art Unit 1631
Lori A. Clow
Patent Examiner